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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/799,326	03/12/2004	Narendra S. Yadav	CL1806USCIP	9215

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EXAMINER

ZHENG, LI

ART UNIT

PAPER NUMBER

1638

DATE MAILED: 06/23/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/799,326	YADAV ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Li Zheng	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 10 April 2006.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1,2,6 and 58-67 is/are pending in the application.
- 4a) Of the above claim(s) 1,2,6 and 58-66 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 67 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 12 March 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |                                                                                                    |                                                                             |
|----------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                        | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)               | Paper No(s)/Mail Date. _____                                                |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>3122004</u>                                                               | 6) <input type="checkbox"/> Other: _____                                    |

## **DETAILED ACTION**

### ***Election/Restrictions***

1. Applicant's election without traverse of Group III, claim 67, and withdrawal of non-elected claims in the reply filed on 4/10/2006 are acknowledged.

Applicants also elected SEQ ID NO:77 and SEQ ID NO: 78.

The requirement is deemed proper and is therefore made FINAL.

Note that since applicant elected SEQ ID NO:77 and SEQ ID NO: 78, the claim 67 is fully supported by parent applications.

### ***Specification***

2. The disclosure is objected to because of the following informalities: the recitation, "a 128 bp PCR product encoding the 111 amino acid", on Page 68, line 23 as well the recitation, " a 588 bp PCR product (CreC) encoding the 564 amino acid", on page 68, line 31, are incorrect since the nucleotide sequences cited can not encode the cited number of amino acids.

Appropriate correction is required. New matter must be avoided.

***Claim Objections***

3. Claim 67 is objected to since it is drawn to non-elected subject matter. For the purpose of examination, the non-elected sequence of SEQ ID NO: 71 is not examined.

4. Claim 67 is objected to since there is a typographical error in recitation, "set for the", in line 5.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claim 67 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

A review of the full content of the specification indicates that to make and use the genus of IntN, SEQ ID NO: 77 and 78 are essential to the operation of the claimed invention.

A review of the language of claim 67 indicates that the claimed method encompasses a broad genus, including any IntN that comprises motif A of SEQ ID NO: 77 and motif B of SEQ ID NO: 78. However, the specification only

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describes an IntN that comprises SEQ ID NO: 77 and SEQ ID NO: 78 and an IntC from dnaE-n and dnaE-c of *Synechocystis* sp. PCC6803, respectively. The specification does not teach how motifs indicated by SEQ ID NO: 77 and 78 are related to the function of IntN. Wu et al (1998, *PNAS* 95:9226-9231) disclose alignment of several IntN and IntC sequences and it, however, shows that no other IntN comprises SEQ ID NO: 78 and 77 (Fig. 2 on page 9228). The only structures correlated in the specification with intein activity are SEQ ID NO: 77 and 78. Given the breadth of the claims, a person skilled in the art would conclude that applicant does not provide adequate description on the genus of IntN comprising SEQ ID NO: 77 and 78.

6. Claim 67 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for combination of IntN and IntC from *Ssp* dnaE of *Synechocystis* sp. PCC6803, does not reasonably provide enablement for all IntNs comprising SEQ ID NO: 77 and 78 with any IntC. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claim is broadly drawn to a method using any IntN comprising SEQ ID NO: 77 and 78 with any IntC. Evans et al (2000, *J. Biol. Chem.* 275:9091-9094) teach that it is important that IntC needs to physically interact with IntN in order to reconstitute the *Ssp* DnaE intein (Fig. 3 on page 9092) for splicing. Given this teaching, it is highly unlikely that any other IntC can physically interact with any

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IntN comprising SEQ ID NO: 77 and 78. Further, the specification admit that Ssp DnaE inteins are the only known naturally split inteins (Page 2, line 26).

Therefore, undue experimentation would be required to determine if what kind of IntC proteins can physically interact with IntN comprising SEQ ID NO: 77 and 78.

Given the breadth of the claim, unpredictability of affinity between a IntN comprising SEQ ID NO: 77 and 78 and any IntC, and lack of further guidance, undue experimentation would have been required for a person skilled in the art to practice the invention in full scope.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of

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35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claim 67 is rejected under 35 U.S.C. 103(a) as being unpatentable over Chen et al (2001, *Gene* 263:39-48) in view of Wu et al (1998, *PNAS* 95:9226-9231) and Whitelam et al. (1993, *Biotechnol. Genet. Eng. Rev* 11:1-29).

The instant claim is drawn to a method for producing a protein comprising an ExtN and a ExtC, said method comprising: a) obtaining an N-nucleotide sequence that encodes an N-polynucleotide comprising an ExtN and an IntN wherein IntN comprising SEQ ID NO: 77 and SEQ ID NO: 78; b) obtaining a C-nucleotide sequence that encodes a C-polynucleotide comprising an IntC and an ExtC; c) transforming a plant host with said plant produces said protein and d) optionally recovering said protein. .

Chen et al. teach that a herbicide resistant gene, EPSPS, is divided into amino acids 1-235 (ExtN) and 236-427(ExtC) which are fused to N-terminal splicing domain (IntN) and C-terminal domain (IntC) of SsP DnaE intein, respectively. Expression of EPSPS-intein fusion proteins in *E.coli* from separate DNA molecules confers resistance to the herbicide glyphosate, indicating that the intein splicing domains are bringing the EPSPS fragments together to generate activity (abstract).

Chen et al. do not teach that N-terminal splicing domain (IntN) of SsP DnaE intein comprises SEQ ID NO: 77 and 78. Chen et al also do not teach the expression of the fusion proteins in plant. However, it is clearly stated by Chen et al that the goal for the research is to control the transgene spread via pollen by

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expressing those two inactive fusion proteins from separate DNA locations, such as nuclear and chloroplast genome. (see last sentence in abstract and also Fig. 6)

Wu et al. teach that N-terminal splicing domain (IntN) of SsP DnaE intein comprises motifs set forth by SEQ ID NO: 77 and 78 (Fig. 2 (B)).

Whitelam et al. (1993, *Biotechnol. Genet. Eng. Rev* 11:1-29) teach heterologous protein production in transgenic plants wherein the protein are either harvested or expressed in plant to modify plant phenotype. Whitelam et al. disclose that many plant species are amenable to plant transformation (page 6, 2<sup>nd</sup> full paragraph). Whitelam et al. also disclose promoters that are operable in plants, such as the CaMV 35S promoter (page 8-9). Whitelam et al. further teach that "there is evidence that efficiency of translation of transgenic mRNA in plants can be increased by modification of the coding sequence of the transgene" (page 11, 1<sup>st</sup> full paragraph).

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the constructs of Chen et al according the teaching of Whitelam et al to express the fusion proteins in plant, thus resulting in the practice of the instantly claimed invention with a reasonable expectation of success. It was obvious that the IntN of Chen et al. comprises SEQ ID NO: 77 and 78, given the teachings of Wu et al. One would have been motivated to express the fusion proteins in plant given the teaching of Chen et al. that transgene spread via pollen may be controlled in the future by expressing those



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two inactive fusion proteins from separate DNA locations, such as nuclear and chloroplast genome, and using the split intein to generate protein activity (see last sentence in abstract and also Fig. 6).

### ***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim 67 is provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 23-31 of copending Application No. 10/356,088 in view of Chen et al (2001, *Gene* 263:39-48) and Wu et al (1998, *PNAS* 95:9226-9231).

Claim 23 of copending Application No. 10/356,088 teaches a method for producing a protein comprising an ExtN and a ExtC, said method comprising: a) obtaining N-nucleotide sequence that encodes an N-polypeptide comprising an

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ExtN and IntN; b) obtaining C-nucleotide sequence that encodes an C-polypeptide comprising an ExtC and IntC; c) transform a plant host with said N-nucleotide sequence and said C-nucleotide sequence such that said plant produce said protein.

Claim 23 of copending Application No. 10/356,088 does not teach that IntN further comprises motif A and B as set forth in SEQ ID NO:77 and 78, respectively, or polypeptide sequence as set forth in SEQ ID NO: 71.

Chen et al. teach that a herbicide resistant gene, EPSPS, is divided into amino acids 1-235 (ExtN) and 236-427(ExtC) which are fused to N-terminal splicing domain (IntN) and C-terminal domain (IntC) of SsP DnaE intein, respectively. Expression of EPSPS-intein fusion proteins in *E.coli* from separate DNA molecules confers resistance to the herbicide glyphosate, indicating that the intein splicing domains are bringing the EPSPS fragments together to generate activity (abstract).

Wu et al. teach that N-terminal splicing domain (IntN) of SsP DnaE intein comprises motifs set forth by SEQ ID NO: 77 and 78 (Fig. 2 (B)).

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to practice the method taught Claim 23 of copending Application No. 10/356,088 by using the constructs of Chen et al thus resulting in the practice of the instantly claimed invention with a reasonable expectation of success. It was obvious that the IntN of Chen et al. comprises SEQ ID NO: 77 and 78, given the teachings of Wu et al. One would have been motivated to express the fusion proteins in plant given the teaching of Chen et al. that

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transgene spread via pollen may be controlled in the future by expressing those two inactive fusion proteins from separate DNA locations, such as nuclear and chloroplast genome, and using the split intein to generate protein activity (see last sentence in abstract and also Fig. 6).

This is a provisional obviousness-type double patenting rejection.

### ***Conclusion***

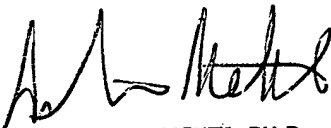
Claim 67 is rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Li Zheng whose telephone number is 571-272-8031. The examiner can normally be reached on Monday through Friday 9:00 AM - 5:30 PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached on 571-272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



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